## REMARKS

### I. PRELIMINARY REMARKS

Claim 55-63 and 65 are pending and are directed to a method for generating a composition of contiguous overlapping peptide fragments for allergen specific immunotherapy to reduce the risk of anaphylaxis. In particular, the invention is directed to the preparation of improved compositions of contiguous overlapping peptide fragments (COPs) for selected allergens wherein the fragments are capable of inducing a T cell response in patients who are hypersensitive to the allergen but wherein administration of the compositions of the invention results in lower levels of IgE stimulation activity.

Also submitted herewith is an amendment of SEQ ID NO: 5 to correct an obvious typographical error. Specifically, amino acids 1 to 90 (namely up to seq ...SVIEGG) is the proper sequence of the Bet v 1 fragment as may be seen by comparison with SEQ ID: 7. Applicants have discovered that part of SEQ ID: 4 (PLA2 sequence) was inadvertently added thereafter, namely starting with HPVT... and ending with ...DLRKY to produce an erroneous sequence.

That there is an error is obvious, and that its solution is the insertion of the sequence of amino acids 91 to 125 of SEQ ID NO: 7 is obvious from a study of SEQ ID NO: 7 presenting the entire sequence of the Bet v 1 amino acid sequence (SEQ ID NO: 7) which presents the correct amino acids for 91 to 125. It is also obvious from a study of SEQ ID NO: 6 which overlaps with both SEQ ID NO: 5 and SEQ ID NO: 7 at amino acid number 81 through amino acid number 125 of those sequences with the sequence "Lys Tyr Asn Tyr Ser..." that SEQ ID NO: 5 should include that same sequence of amino acids through amino acid 125. Finally, a review of SEQ ID NO: 4 which is to a completely different antigen ($PLA_2$ not Bet v 1) demonstrates the erroneous nature of SEQ ID NO: 5 as filed.

### II. OUTSTANDING REJECTIONS

Claims 55-61 and 63 stand rejected under 35 U.S.C. §102(b) as being anticipated by WO 01/88085.

Claims 55 and 61-62 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 in view of Shanti et al., The Journal of Immunology, Vol. 151, 5354 5363, No. 10, 11/15/1993.

Claims 55, 63 and 65 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 in view of Spertini et al., C23 Abstract AAAI presented at AAAAI (Am. Acad. Allergy Asthma and Immunol.) San Diego, March 3-8, 2000, and published in J. Allergy Clin. Immunol., 105(1- pt. 2):S278.

III. Patentability Arguments

A. The Rejections of Claims 55-61 Under 35 USC §102 Over WO 01/88085 Should Be Withdrawn.

The anticipation rejection of claims 55-61 over WO 01/88085 should be withdrawn because the reference discloses some of the individual elements of independent claim 55 but fails to disclose their combination in the order and manner of the invention to yield an improved method for generating contiguous overlapping peptides (COPs).

The concept of COPs is in the prior art and it is the case that COPs useful for immunotherapy to reduce the risk of anaphylaxis from a particular allergen will share certain characteristics. Specifically, useful COPs have been identified empirically in the past and are characterized by possessing the properties of having T cell stimulating activity for T cells specific for the selected allergen but having weak binding activity for IgE's reactive with the selected allergen.

While WO 01/88085 discloses overlapping polypeptide fragments and the fact that useful COPs are characterized by strong T cell stimulating activity and weak IgE reactivity, it does not disclose a systematic method by which useful COPs can be identified. What the Applicant has contributed is a systematic method by which useful COPs can be identified and generated for a polypeptide allergen. Thus, the first steps of Applicant's invention are (1)(a) conducting a structural analysis to identify three dimensional structural formations of the allergen followed by (1)(b) selecting one or more separation sites within the sequence of the

polypeptide allergen to provide COPS presenting T-cell structural motifs but not tertiary structural motifs such that the overlapping peptide fragments do not bind or weakly bind IgE.

The Action cites to portions of WO 01/88085 relating to polypeptide fragments of various lengths (page 2) and that proteins or variant peptides "can tolerize or anergize appropriate T-cell subpopulations" (page 19, lines 14-15). However, the reference does not teach the element of "selecting separation sites" to produce COP's presenting "potential T-cell epitopes but not alpha helix and beta-sheet structural motifs..." as claimed. In fact, WO 01/88085 states only that the administration of its Api m 6 proteins, peptides or variants "may result in lower levels of IgE stimulation." (page 19, lines 25-26, emphasis supplied) This indicates a hit or miss quality to the prior art method which does not disclose the claimed element of affirmatively selecting separation sites whereby lower levels of IgE would be obtained.

The reference also fails to disclose screening candidate COPs according to the invention. Specifically, WO 01/88085 discloses testing a peptide for T-cell stimulating activity but does not discloses testing a composition of COPs (that is multiple peptides) for such activity. Similarly, WO 01/88085 discloses testing of peptides for IgE-mediated immune responses fails to disclose testing of COPs or the screening and selecting of Cops having a greater than minimum T cell stimulating activity and a less than a selected maximum of IgE binding activity.

Thus, while WO 01/88085 discloses or nearly discloses many of the elements of the claims those elements are not the same as or arranged in the same order as those elements are recited in claim 55 and it fails to disclose the method of claim 55 as a whole.

B. The Rejections of Claims 55, and 61-62 Under 35 USC §103(a) in view of Spertini WO 01/88085 in view of Shanti et al. Should Be Withdrawn.

The rejection of claims 55 and 61-62 under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 in view of Shanti et al. (The Journal of Immunology, Vol. 151, 5354-5363, No. 10, 11/15/1993) should be withdrawn because Shanti fails to make up for the deficiencies of WO 01/88085 with respect to independent claim 55 as described above. More specifically, Shanti fails to teach the overall method of identifying compositions of COPs and while WO 01/88085 and Shanti individually disclose many (but not all) of the elements of claim 55 they do not teach all the steps or the method as a whole. Accordingly, the rejection of claims 55 and 61-62 should be withdrawn.

C. The Rejections of Claims 55 and 63-65 Under 35 USC §103(a) in view of Spertini et al. WO 01/88085 in View of Spertini C23 Should Be Withdrawn.

The rejection of claims 55 and 63-65 under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 in view of Spertini et al. C23 Abstract AAAI presented at AAAAI (Am. Acad. Allergy Asthma and Immunol.) San Diego, March 3-8, 2000, and published in J. Allergy Clin. Immunol., 105(1- pt. 2):S278 should be withdrawn because Spertini C23 neither makes up for the deficiencies of WO 01/88085 with respect to the elements of independent claim 55 nor does it teach the elements of dependent claims 63-65 directed to the specifics of the dermal test.

More specifically, Spertini C23 fails to teach the overall method of identifying compositions of COPs and while WO 01/88085 and Spertini C23 individually disclose many (but not all) of the elements of claim 55 they do not teach all the steps or the method as a whole. Accordingly, the rejection of claims 55 and 61-62 should be withdrawn.

## CONCLUSION

For the foregoing reasons, it is submitted that each of claims 55-63 and 65 should now be allowed. Should the Examiner wish to discuss any issues of form or substance, he/she is invited to contact the undersigned attorney at the number below.

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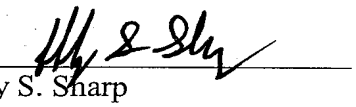
Respectfully submitted,

By 

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